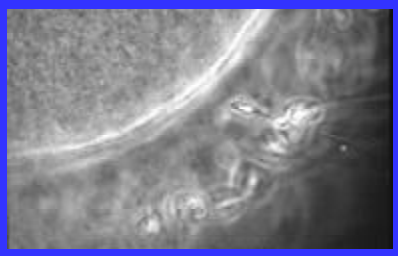
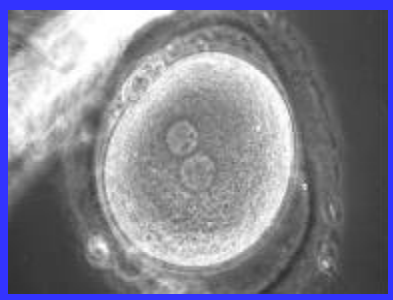
Evidence-Based Human ART: statements by Barry Bavister, Ph.D.

Credentials:

- PhD in Reproductive Biology, Cambridge University, 1972
- Author/co-Author >200 publications in embryology (many with non-human primates)
- Research continuously funded by NIH 1979-2002
- Member, National Cooperative Program on Non-Human in Vitro Fertilization and Embryo Development, 1986-2000
- Professor, University of Wisconsin-Madison, 1979-2000
- Endowed Chair in Reproductive Biology, University of New Orleans, 2000 - present
- President, International Embryo Transfer Society





First human IVF eggs

Bavister, Edwards and Steptoe (1969) Identification of the midpiece and tail of the spermatozoon during fertilization of human eggs in vitro. *J. Reprod. Fertil.* 20:159-160.

Edwards, Bavister and Steptoe (1969) Early stages of fertilization in vitro of human oocytes matured in vitro. *Nature (Lond.)* 221:632-635.

Petri at about 5 years old

First non-human primate IVF protocols and first documented NHP offspring

Bavister *et al.* (1983) Fertilization and cleavage of rhesus monkey oocytes in vitro. *Biol. Reprod.* 28:983-999.

Bavister *et al.* (1984) Birth of rhesus monkey infant after in vitro fertilization and non surgical embryo transfer. *Proc. Natl. Acad. Sci. U.S.A.* 81:2218-2222.

Estimated Efficiency of Human IVP by Denominator

Denominator	n	CPR %	LBR %
Transfer procedure	**1**	**35***	**29***
Embryos transferred	3	12	10
Embryos >2-cells	10	3.5	3
Ova fertilized	12	3	2.5
Oocytes retrieved & inseminated	15	2.5	2

*SART Report, 1998: women = 37 years; 31/25% = 40

Some Key Differences in Reproductive Strategies between Rodents vs. Primates

- maternal (rodents) vs. paternal (primates) centriolar inheritance
- site of block to polyspermy different in mouse vs. primates
- cell cycle timing of embryonic genome activation
- cell cycle regulation of metabolic changes in embryo
- implantation: embryonal pole and invasive in primates
- maternal recognition of pregnancy - CG secretion in primates
- multiple implantations (litter-bearing) in rodents
- reproductive senescence and high aneuploidy rates in primates
- estrous vs. menstrual cycles; reproductive endocrinology

Because of the great diversity in reproductive strategies among mammals, in many fundamental respects mice are unsuitable models for human embryology and reproduction; the most suitable models are **non-human primates**

- United States non-human primate research infrastructure; little utilized for reproductive research
- NIH study sections rarely fund primate reproduction proposals; divert excessive resources to mouse research

Consequences and Conclusions

- Little is known about primate embryology
- Almost no embryology research is being supported in the U.S. that can be directly applied to human ART
- In the U.S. there is a huge gulf between animal and human reproductive biology
- Human ART is being conducted in the virtual absence of animal-based evidence

ART areas urgently needing research using non-human primates

- embryo stem cell biology
- cytoplasmic transplantation/ mitochondrial heteroplasmy
- oocyte “GV nucleus” transplantation
- culture media formulations for blastocysts
- oocyte maturation and cryopreservation

Solutions:

- The U.S. should support major initiatives in non-human primate embryology and reproductive research, utilizing superior resources of the federal Primate Centers
- In addition, efforts should be made to bring the U.S. scientific and clinical-reproductive communities together